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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/027,484	12/21/2001	Sebastian Bohm	TGZ-001B	9951
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LAHIVE & COCKFIELD, LLP. 28 STATE STREET BOSTON, MA 02109			EXAMINER BARTON, JEFFREY THOMAS	
			ART UNIT 1753	PAPER NUMBER

DATE MAILED: 10/27/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/027,484

Applicant(s)

BOHM ET AL.

Examiner

Jeffrey T. Barton

Art Unit

1753

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 August 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-69 is/are pending in the application.
- 4a) Of the above claim(s) 2-8, 22-41, 49-54, 59, 60 and 67-69 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 9-21, 42-48, 55-58 and 61-66 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 30 September 2002 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 20030728, 20030224.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☒ Other: IDS 20020723, 20020708.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I (Claims 1-21 and 42-66) in the reply filed on 08/05/2004, and of Species A (Claims 1, 9-21, 42-48, 55-58, and 61-65) in the interview of 8/30/2004 are acknowledged. The traversal is on the grounds that: all claims are linked by a unifying aspect (fluid introduction to a microchannel through a port formed in the sidewall of the channel) and the search of all claims would not result in a serious burden to the examiner. This is not found persuasive because the linking aspect of fluid introduction through an interface port in the sidewall of a microchannel was not found to be patentable (see rejections below), and the disparate embodiments claimed (e.g. liquid-liquid extraction, sample separation, fluid injection, and processing with chemical reaction) are classified separately, each requiring a distinct search.

The requirement is still deemed proper and is therefore made FINAL.

Drawings

2. The drawings are objected to as failing to comply with 37 CFR 1.84(p)(5) because.
3. The drawings are objected to because of the following informalities:
 - a. Apparent mislabeling of targeting electrode 61 (Page 29, lines 4, 6) as 60 in Figure 11c.
 - b. The drawings do not include the following reference sign(s) mentioned in the description: 57 (Fig. 11A), 17 (Fig. 11B), 181 (Fig. 18)

c. In figure 9f, the top of the encapsulant is labeled as virtual wall 15. For consistency, the lower meniscus in this figure should be labeled as the virtual wall. This change would also be more consistent with the specification. (Page 26, lines 1-7)

Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. The replacement sheet(s) should be labeled "Replacement Sheet" in the page header (as per 37 CFR 1.84(c)) so as not to obstruct any portion of the drawing figures. If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Claim Objections

4. Claim 56 is objected to because of the following informalities: unclear antecedent basis. This claim specifies "moving the fluid in the microchannel," while

claim 42, on which it depends, refers to both a "first fluid" and "second fluid." The claim is treated herein as requiring motion of any fluid in the microchannel. Appropriate correction is required.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1, 42, 48, 56, 58, 64, and 65 are rejected under 35 U.S.C. 102(b) as being anticipated by Howitz et al.

Addressing claims 1 and 42, Howitz et al disclose a method of injecting a second liquid into a microchannel filled with a first liquid (Figure) comprising: forming a droplet from the second liquid (Figure, droplet 5) and directing the droplet to, and introducing it through a virtual wall formed by the first fluid in a fluid interface port (6) formed in a sidewall of the microchannel (9). (Column 2, line 65 - Column 3, line 34)

Addressing claim 48, Howitz et al disclose the droplet traversing the virtual wall. (Column 3, lines 31-34) As such, its speed and direction must be appropriate.

Addressing claim 56, Howitz et al disclose fluid motion in the microchannel. (Column 2, lines 1-37)

Addressing claim 58, Howitz et al disclose a droplet having a diameter smaller than the fluid interface port. (Figure)

Addressing claim 64, Howitz et al disclose a method of injecting a second liquid into a microchannel filled with a first fluid, said method comprising: forming a droplet (5) from the second liquid, introducing said droplet through a virtual wall formed by the first fluid in a fluid interface port (6) formed in a sidewall of the microchannel (9), said fluid interface port having a diameter between about 25 μm and about 100 μm . (Column 2, line 65 - Column 3, line 34)

Addressing claim 65, Howitz et al disclose a method of injecting a second liquid into a microchannel filled with a first fluid, said method comprising: forming a droplet (5) from the second liquid, introducing said droplet through a virtual wall formed by the first fluid in a first fluid interface port (6) formed in a sidewall of the microchannel (9), wherein the microchannel is free of a second coaxially arranged fluid interface port formed in the sidewall at a location opposite to the first fluid interface port. (Column 2, line 65 - Column 3, line 34)

7. Claims 9-12, 14, 15, 20, and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Columbus. (US 4,302,313)

Relevant to claim 9, Columbus discloses a method of filling a microchannel, comprising directing fluid droplets through an interface port in the channel sidewall (Column 13, lines 30-34), such that the liquid traverses the port and enters the interior. (Column 13, line 42 - Column 14, line 16)

Relevant to claim 10, Columbus discloses the port being a filling aperture.
(Column 13, lines 66-68)

Relevant to claims 11 and 12, Columbus discloses a pressure barrier formed in the microchannel to force the liquid in a first direction. (Figure 19, wider zones 220 force fluid to fill narrower portions of the channel) These widened portions can be called, "stopper holes."

Relevant to claim 14, Columbus discloses vent holes through the sidewall.
(Column 14, lines 59-68)

Relevant to claim 15, Columbus discloses continued fluid introduction and transport until the channel is filled with liquid. (Figures 20a-c; Column 14, lines 22-40)

Relevant to claim 20, Columbus discloses filling the channel with two fluids introduced into separate filling apertures, each according to the method of claim 9.
(Figures 20 a-c; Column 13, line 30 - Column 14, line 16)

Relevant to claim 21, Columbus discloses introduction of a gelatinous solution that would not be miscible with an introduced sample fluid. (Column 10, lines 4-41)

8. Claims 9, 10, 14, 15, 42, and 55 are rejected under 35 U.S.C. 102(b) as being anticipated by Columbus. (US 4,426,451)

Relevant to claim 9, Columbus discloses a method of filling a microchannel (Figures 1 and 2), comprising directing fluid droplets through an interface port in the channel sidewall (Column 5, lines 24-28), such that the liquid traverses the port and enters the interior. (Column 4, line 55 - Column 5, line 43)

Relevant to claim 10, Columbus discloses the port being a filling aperture.
(Column 5, lines 24-28)

Relevant to claim 14, Columbus discloses vent holes through the sidewall.
(Figure 2, hole 50)

Relevant to claim 15, Columbus discloses continued fluid introduction and transport until the channel is filled with liquid. (Figure 2, channel 22 is filled)

Relevant to claim 42, Columbus discloses introduction of a second fluid into a microchannel filled with a first fluid by directing a second liquid to a virtual wall formed in an interface port by the first fluid. (Figures 2-3; Column 7, lines 59-60)

Relevant to claim 55, Columbus discloses this second fluid being immiscible with the first. (Column 7, lines 59-60)

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

10. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claim 13 is rejected under 35 U.S.C. 103(a) as being unpatentable over Columbus (US 4,302,313) in view of Columbus. (US 4,426,451)

Columbus (US 4,302,313) discloses methods as described above in addressing claims 11 and 20.

Columbus (US 4,302,313) does not explicitly disclose disposition of a hydrophobic patch in the channel to form a pressure barrier (Claim 13).

Columbus (US 4,426,451) discloses using a hydrophobic surface to prevent fluid flow into a region of his device. (Column 8, line 54 - Column 9, line 22)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method of Columbus (US 4,302,313) by performing it

in a device that uses a hydrophobic surface to control fluid flow, as taught by Columbus (US 4,426,451), because Columbus (US 4,426,451) teaches its effectiveness in preventing flow to undesired areas of the device, which is required in the method of Columbus. (US 4,302,313; Column 14, lines 29-40)

13. Claims 16 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Columbus (US 4,302,313) in view of Kopf-Sill. (US 6,420,143)

Columbus discloses a method as described above in addressing claim 9.

Columbus does not explicitly disclose closing the fluid interface port after filling the channel (Claim 16) or closing the port with a fluid encapsulant. (Claim 17)

Kopf-Sill discloses sealing a fluid reservoir in a microfluidic device with mineral oil in order to reduce evaporative losses. (Column 8, lines 25-30)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method of Columbus by adding a liquid encapsulant to the fluid inlet port to seal it after the fluid filling step, as taught by Kopf-Sill, because it would reduce evaporation losses and contamination in analyses run for a length of time or at a temperature where they would be a concern.

14. Claims 16, 18, and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Columbus (US 4,302,313) in view of Swierkowski.

Columbus discloses a method as described above in addressing claim 9.

Columbus does not explicitly disclose closing the fluid interface port after filling the channel (Claim 16) or closing the port with a covering layer or adhered covering layer. (Claims 18 and 19)

Swierkowski discloses sealing fluid reservoirs in a microfluidic device with an adhesive film in order to reduce contamination and evaporative losses. (Column 2, line 67 - Column 3, line 9)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method of Columbus by covering the fluid inlet ports with an adhesive covering layer in order to seal them after the fluid filling step, as taught by Swierkowski, because it would reduce evaporation losses and contamination in analyses run for a length of time or at a temperature where they would be a concern.

15. Claims 42, 43, 61, and 62 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sundberg et al in view of Howitz et al.

Relevant to claim 42, Sundberg et al disclose a method of introducing a fluid into a microchannel comprising forming a droplet of the fluid and introducing it to the channel via a fluid interface port.

Relevant to claim 43, Sundberg et al disclose the fluid port comprising a second port arranged coaxially with the first, directly opposite. (Figures 2 and 3; Column 5, line 64 - Column 6, line 25)

Relevant to claim 61, Sundberg et al disclose forming the droplet on a droplet-carrying element. (Figure 2)

Relevant to claim 62, Sundberg et al disclose applying the droplet to the port with the droplet-carrying element.

Sundberg et al do not explicitly disclose the droplet being introduced through a virtual wall formed by a fluid already disposed within the channel, or the droplet being introduced to the virtual wall by the droplet-carrying element.

Howitz et al disclose addition of droplets of fluid through a virtual wall into a channel already filled with a fluid.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method of Sundberg et al by introducing the fluid via a virtual wall in the port into a channel already filled with fluid, as taught by Howitz et al, because it would allow facile dosing of additional liquids into the device.

16. Claims 44 and 45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sundberg et al and Howitz et al as applied to claim 42 above and further in view of Swedberg et al.

Sundberg et al and Howitz et al disclose a combined method as described above in addressing claim 42.

Neither Sundberg et al nor Howitz et al explicitly disclose any specific means of detection within their device.

Swedberg et al disclose a microfluidic device that includes apertures through the substrates that define the channels to enable optical detection. (Column 17, line 31 - Column 18, line 18)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the combined method of Sundberg et al and Howitz et al by providing optical detection means with a beam directed at the aperture giving access to the channel interior, as taught by Swedberg et al, because such a beam path would minimize absorbance or distortion by the device material.

17. Claims 44 and 45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Howitz et al in view of Swedberg et al.

Howitz et al disclose a method as described above in addressing claim 42.

Howitz et al do not explicitly disclose any specific means of detection within their device.

Swedberg et al disclose a microfluidic device that includes apertures through the substrates that define the channels to enable optical detection. (Column 17, line 31 - Column 18, line 18)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method disclosed by Howitz et al by providing optical detection means with a beam directed at the aperture giving access to the channel interior, as taught by Swedberg et al, because such a beam path would minimize absorbance or distortion by the device material.

18. Claims 46, 47, 63, and 66 are rejected under 35 U.S.C. 103(a) as being unpatentable over Howitz et al.

Howitz et al disclose a method as described above in addressing claim 42. They also suggest introduction of plural fluids through the interface ports of their device. (Column 1; repeated mention of a fluid microdiode permeable to *fluids* (italics added))

Howitz et al do not explicitly describe the dead volume within the interface ports (Claims 46, 47, and 66) or the introduction of a second droplet of a third fluid through a virtual wall in a second interface port. (Claim 63)

Regarding claims 46, 47, and 66, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method disclosed by Howitz by performing it in a device wherein the interface port has no dead volume or dead volume of less than a nanoliter, because this dead volume is simply a function of the affinity of the fluid within the channel for the walls of the port, fluid surface tension, and the respective pressures of the liquid and gas at the interface. Howitz discusses such variability of meniscus formation (Column 3, lines 25-31), and choice of fluids, pressures, and materials would allow minimization or elimination of the dead volume.

Regarding claim 63, it would also have been obvious to one having ordinary skill in the art at the time the invention was made to use the invention of Howitz for the introduction of plural fluids to the fluid-filled channel, because it is suggested by Howitz and combination of multiple fluids is a common process requirement.

19. Claims 57, 61, and 62 are rejected under 35 U.S.C. 103(a) as being unpatentable over Howitz et al in view of Sundberg et al.

Howitz et al disclose methods as described above in addressing claim 42 and 56.

Howitz et al do not explicitly disclose causing fluid motion by electric fields (Claim 57), forming the droplet on a droplet-carrying element (Claim 61), or introducing the droplet to the virtual wall on a droplet-carrying element. (Claim 62)

Sundberg et al disclose fluid motion being caused by application of an electric field (Column 6, lines 26-33), formation of droplets on a carrying element prior to introduction to a channel (Figure 2), and introduction of the droplet to the port via the carrying element. (Column 5, lines 32-34)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method disclosed by Howitz et al by causing fluid motion by application of an electric field, as taught by Sundberg et al, because it is a reliable means of causing fluid motion in a channel.

It would also have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method disclosed by Howitz et al by forming droplets on pins and introducing the droplets to the ports on these pins, as taught by Sundberg et al, because it is a controllable, reliable fluid transfer means.

Conclusion

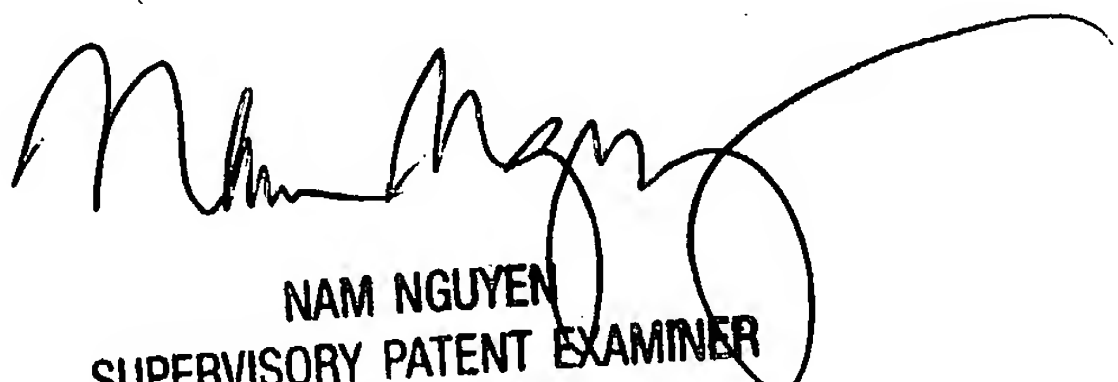
20. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Nakajima et al disclose a device including droplet introduction to a channel through ports. The additional Columbus references disclose related devices and methods to those cited above.

21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Jeffrey Barton, whose telephone number is (571) 272-1307. The examiner can normally be reached Monday-Friday from 8:30 am – 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nam Nguyen, can be reached at (571) 272-1342. The fax number for the organization where this application or proceeding is assigned is (703) 872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at (866) 217-9197 (toll-free).

JTB
October 20, 2004



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